

In the Claims:

Please cancel claim 20.

Please amend claims 7, 9-12, 14 and 16-19 as follows:

1. (Canceled)

2. (Canceled)

3. (Canceled)

4. (Canceled)

5. (Canceled)

6. (Canceled)

7. (Currently Amended) A method to identify a compound that inhibits ~~wild-type~~ full length aggrecanase metalloprotease enzymatic activity comprising the steps of:

contacting a test compound, a truncated aggrecanase, said truncated aggrecanase comprising a metalloprotease domain, and a peptide substrate, said peptide substrate being less than 40 amino acids in length, wherein the peptide substrate comprises a cleavage site between a glutamic acid on an N-terminal side of the cleavage site and a non-polar or uncharged amino acid residue on a C-terminal side of the cleavage site and wherein the peptide substrate is cleavable by said truncated aggrecanase; and

detecting cleavage of the peptide substrate, wherein inhibition of peptide substrate cleavage in ~~the~~ a presence of a test compound indicates compound inhibition of ~~wild-type~~ full length aggrecanase metalloprotease enzymatic activity.

8. (Original) The method of claim 7 wherein the method is conducted in a single reaction vessel.

9. (Currently Amended) The method of claim 7 wherein the ~~wild-type~~ full length aggrecanase enzyme is selected from the group consisting of aggrecanase-1 and ~~aggrenase-2~~ aggrecanase-2.

10. (Currently Amended) The method of claim 7 wherein the peptide substrate is selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO: 5, SEQ ID NO:6 and SEQ ID NO:7.

11. (Currently Amended) The method of claim 7 wherein the peptide substrate further comprises a detectable label selected from the group consisting of ^{125}I , ^{131}I , ^3H , ^{14}C , ^{35}S , ^{32}P , ^{33}P , a fluorescent dye, and a colorimetric indicator.

12. (Currently Amended) The method of claim 7 wherein the peptide substrate further comprises a fluorophore and a quencher or acceptor located at opposite ends of the cleavage site of the peptide.

13. (Previously Amended) The method of claim 7 wherein the truncated aggrecanase is in a cell expressing the truncated aggrecanase.

14. (Currently Amended) A method to detect ~~the ability of a compound to inhibit~~ wild-type inhibition of metalloprotease enzymatic activity of full length aggrecanase-1 or -2 ~~enzymatic activity~~ comprising the steps of:

~~contacting a test compound,~~ combining a truncated aggrecanase secreted by a cell, said truncated aggrecanase comprising a metalloprotease domain, ~~and~~ a peptide substrate having a detectable label and an amino acid sequence selected from the group consisting of SEQ ID NO:3 and SEQ ID NO:4 in a presence or an absence of a test compound;

incubating the test compound, the truncated aggrecanase and the peptide substrate to ~~permit enzymatic cleavage of the peptide~~ produce a detectable product as a result of metalloprotease enzymatic activity upon the peptide substrate; and

measuring a quantity of product formed in a presence of the test compound
and in an absence of the test compound, whereby the inhibition is detected when an amount
of product formed in the presence of the test compound is less than that in the absence of the
test compound.

~~measuring enzymatic cleavage of the peptide;~~

~~wherein said measuring involves determining presence or absence of cleavage~~
~~of said peptide.~~

15. (Original) The method of claim 14 wherein the peptide comprises a detectable label selected from the group consisting of ^{125}I , ^{131}I , ^3H , ^{14}C , ^{35}S , ^{32}P , ^{33}P , a fluorescent dye, or a colorimetric indicator.

16. (Currently Amended) The method of claim 14 wherein the peptide substrate comprises a fluorophore and a quencher or acceptor located at opposite ends of the cleavage site of the peptide substrate.

17. (Currently Amended) A method to identify a compound capable of inhibiting ~~wild-type~~ full length aggrecanase activity comprising the steps;

providing a peptide substrate comprising an affinity moiety, an amino acid sequence selected from a group consisting of SEQ. ID NO:3 and SEQ ID NO:4 and a detectable label, said affinity moiety and label located on opposite sides of a cleavage site encoded by the amino acid sequence;

contacting the peptide substrate with an affinity capture coated solid phase support for sufficient time to bind a portion of the peptide substrate;

washing the support to remove unbound peptide substrate;

contacting a solution comprising a test compound and ~~functional enzyme~~ truncated
aggrecanase comprising a metalloprotease domain with the peptide substrate bound solid

phase support for sufficient time to allow enzymatic cleavage of the peptide substrate,
thereby releasing the peptide substrate and detectable label into the solution; and
measuring changes in the quantity of the detectable label as a result of compound
modulation of expected enzymatic function.

18. (Currently Amended) The method of claim 17 wherein the ~~enzyme~~ full length
aggrecanase is selected from the group consisting of ~~wild-type~~ full length aggrecanase-1 and -
2.

19. (Currently Amended) The method of claim 17 wherein the peptide substrate
comprises a detectable label selected from the group consisting of ^{125}I , ^{131}I , ^3H , ^{14}C , ^{35}S , ^{32}P ,
 ^{33}P , a fluorescent dye, or a colorimetric indicator.

20. (Cancelled)

21. (Previously Amended) The method of claim 7, wherein said truncated
aggrecanase is selected from the group consisting of SEQ ID NO: 8 and SEQ ID NO:9 and
homologues thereof.